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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
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1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,980	AMALFITANO ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-9 and 12-142* is/are pending in the application.

4a) Of the above claim(s) *8,16,24,25,29,34 and 37-142* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,9,12-15,17-23,26-28,30-33,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicants' amendment dated August 22, 2008, to the non-final action dated February 22, 2008, has been entered. Claim 1 and 15 have been amended, and claims 4, 10 and 11were cancelled. No claims were newly added. Accordingly, claims 1-3, 5-9, and 12-142 are pending in the application. Claims 8, 16, 24, 25, 29, 34 and 37-142 stand withdrawn from further consideration, without traverse, as drawn to non-elected inventions and species of the invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. The claims have been examined commensurate in scope with the elected invention, and the species of the invention.

Claims 1-3, 5-7, 9, 12-15, 17-23, 26-28, 30-33, 35 and 36 are under current examination.

Response to & Maintained Objection to the Specification/Abstract

The abstract stands objected to for exceeding 150 words in length and including legal phraseology. The objection set forth on page 3 of the previous office action dated February 22, 2008 is maintained. Applicants have supplied a new abstract, showing markups, including the deleted text of the old Abstract, on the same page, without presenting a clean copy apart from other text.

A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text, in accordance with 37 CFR 1.52(b)(4).

Response to Objections to the Oath/Declaration

The Oath/Declaration was objected in the previous office action dated February 22, 2008, for claiming benefit of priority to U.S. Provisional Application No. 60/376,397, under 35 USC §

119(a)-(d), or (f) of 365(a) or (b), instead of 35 USC § 119(e). Applicants' arguments that the presence of the Cross Reference paragraph in the PCT Application, and the instant specification is sufficient to comply with the requirements of MPEP 201.11, is found persuasive. Accordingly, the previous objection is hereby withdrawn.

New Claim Rejections - 35 USC § 112- New Matter

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claim 15 is newly rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art (hereafter the Artisan), that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR §1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claim 15 has been amended to recite "a helper cell that complements the deletions in the adenovirus vector genome, and further wherein the helper cell provides AAV rep and Cap". However, the newly added limitation of "and further wherein the helper cell provides AAV rep and Cap", in conjunction with the helper cell with the ability to complement deletions in the adenovirus vector genome is not supported by the specification's disclosure. The newly introduced limitation reads on a helper or packaging cell that simultaneously provides for both adenovirus vector and AAV vector viral replication and packaging.

Applicants state that support for the amendment can be found at page 6, lines 19-21, and at page 23, lines 23-24. However, the as-filed specification while providing for 293 cells transfected with plasmids containing the AAV rep and cap genes, is silent in its disclosure of the claimed helper cells that simultaneously provides for both adenovirus vector and AAV vector viral replication. Thus, at the time the application was filed, an Artisan of skill would not recognize from the disclosure that Applicant was in possession of a helper cell that complements deletions in the adenovirus vector genome, and further provides AAV Rep and Cap, as claimed.

MPEP 2163.06 notes: "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re*

Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

This is a new matter rejection.

Response & Withdrawn Claim Rejections - 35 USC § 102

Claims 1-4, 12, 15, 17-22, 26, 27, 35 and 36 were rejected under 35 U.S.C. 102(b) as being anticipated by Lieber et al. (J. Virol. 73(11):9314-9324; 1999), in the previous office action dated February 22, 2008. The cancellation of claim 4 renders its rejection moot. Applicants have amended base claim 1 to incorporate the limitation of a functional adenovirus E4orf6 region, not specifically taught by Lieber et al. Thus, the rejection is hereby withdrawn. The claims are however subject to new rejections over the prior art, as set forth below.

Claims 1-3, 5-7, 9-13, 15, 17-22, 26, 27, 35 and 36 were rejected under 35 U.S.C. 102(e) as being anticipated by Mountz et al. (U.S. Patent No.: 6,383,794, filed Aug. 24, 1999), as evidenced by Samulski et al. (J. Virol. 63(9):3822-3828; 1989), in the previous office action dated February 22, 2008. The cancellation of claims 10 and 11 renders their rejection moot. Applicants have amended base claim 1 to incorporate the limitation of an AAV vector genome that does not encode the AAV Rep or AAV capsid proteins, not specifically taught by Mountz et al. Thus, the rejection is hereby withdrawn. The claims are however subject to new rejections over the prior art, as set forth below.

Response & Withdrawn Claim Rejections - 35 USC § 103

Claims 1, 26-28 and 30-33 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lieber et al. (J. Virol. 73(11):9314-9324; 1999), in view of Podsakoff et al. (U.S. Patent No.: 5,962,313; effective filed Jan. 16, 1997), in the previous office action dated February 22, 2008.

Claims 1 and 21-23 were rejected under 35 U.S.C. §103(a) as being unpatentable over Lieber et al. (J. Virol. 73(11):9314-9324; 1999, of record), in view of Souza et al. (U.S. Patent Application Publication No.: 2003/0017139; effective filed Nov. 16, 1999) , in the previous office action dated February 22, 2008.

Applicants have amended base claim 1 to incorporate the limitations of a functional adenovirus E4orf6 region, and an AAV vector genome that does not encode the AAV Rep or AAV capsid proteins, not specifically taught by the references of Lieber et al., Podsakoff et al, and Souza et al. Thus, the rejections are hereby withdrawn. The claims are however subject to new rejections over the prior art, as set forth below.

New Claim Rejections - 35 USC § 103

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 1-3, 5-7, 9, 12-15, 17-22, 26, 27, 35 and 36 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Lieber et al. (J. Virol. 73(11):9314-9324; 1999), in view of Mountz et al. (U.S. Patent No.: 6,383,794, filed Aug. 24, 1999).

The claims embrace a recombinant adenovirus/AAV hybrid virus comprising an adenovirus vector genome deleted in the polymerase region, or the preterminal protein region, or both; comprising AAV2 inverted terminal repeats (ITRs) and cis-elements for viral replication, packaging and encapsidation, and a functional adenovirus E4orf6 region, further comprising a heterologous nucleic acid sequence, and wherein the AAV genome does not encode the AAV rep or AAV capsid proteins, and wherein the vector genome encodes an AAV rep protein operably

linked to the AAV p5 promoter; and wherein the hybrid virus can complete viral replication in a helper cell that provides AAV Rep and Cap.

Lieber et al. describe integrating adenovirus-AAV hybrid vectors devoid of all viral genes (Title). Further teaching that ITRs inserted into adenovirus (Ad) vector genomes resulting in vector genomes devoid of all viral genes, are efficiently packaged into functional Ad capsids (Abstract). The Ad vectors contain AAV ITRs flanking a reporter gene cassette inserted into the E1 region; Ad.AAV vector genomes contain only the transgene flanked by AAV ITRs, and packaging signals (Abstract; the reporter transgene corresponding to a heterologous nucleic acid, limitation of claim 1(b)).

In Figure 1, Lieber et al. depict an Ad.AAV2 hybrid vector comprising a neo gene under the control of the SV40 and Tn5 promoters (limitation of claims 21, 22 and 27). As the hybrid vector genome does not include coding sequence for any adenoviral or AAV proteins, it necessarily comprises deletions of the adenovirus polymerase and preterminal protein regions (limitation of claims 17-20); and does not encode AAV Rep or AAV capsid proteins (limitation of claim 1 (b)), or E1 region products (limitation of claims 12 and 14). Lieber et al. additionally teach hybrid vectors containing the AAV2 genome ITRs (second column, p. 9315, Figure 1, and first column, first paragraph, p. 9317; limitation of claim 3).

With regard to replication and production of hybrid virus in a helper cell, Lieber et al teach that viruses with different transgene cassettes incorporated into their E1 regions were generated by recombination of pXCJL1-derived shuttle plasmids and pJM17 (Microbix) in 293 cells; thus constituting a helper cell. Viruses containing two AAV ITRs tended to have deletions within the ITRs or other Ad sequences and to recombine with Ad sequences present within the 293 cell genome. Only plaques from viruses with intact ITRs were amplified, CsCl banded, and tittered (first column, p. 9315, under Adenoviruses; limitation of claims 35 and 36).

While Lieber et al. do not describe their hybrid virus as comprising a functional E4orf6 region, such variation in the construction of AAV hybrid vectors was known in the prior art.

Mountz et al. disclose high titer recombinant AAV hybrid vectors encoding a therapeutic gene flanked by ITRs of AAV and the AAV rep and cap genes (Abstract). In Example 1, Mountz

et al. describe the construction of the hybrid Ad-AAV vector, by cloning the 4.2 kb Xba fragment fragment of AAV pSub201 containing the AAV rep and cap genes into the E1 Xba site of an adenoviral shuttle vector (column 13). The pSub201 is an infectious clone of AAV type 2 DNA. The rep and cap genes are under the control of the AAV p5 promoter in the hybrid AdAAV vector, as shown in Fig. 1A (column 4; limitation of claims 6 and 7).

The recombinant AAV further comprises the adenoviral ITRs and an adenovirus packaging signal, El, E2A, E4 and VIA regions and no other adenoviral gene regions (see Fig. 15B, pages 42-44; limitation of claims 2). Mountz et al. state: "Preferably, the adenovirus genome is deleted for all coding sequences other than those genes required for adenoviral replication. More preferably, the genes required for adenoviral replication, and hence remaining on the adenoviral genome, are E1A, E1B, E2A, E4 and VIA." (column 7, last paragraph; limitation of claim 10). As the recombinant hybrid vector does not contain an E2B region, it necessarily is deficient in sequences encoding the preterminal and polymerase protein regions (limitation of claims 1(a) and 17-20). Further, the E4 region contains the E4orf6 (limitation of claim 1(a)), thus curing the deficiency in Lieber et al. The insertion of the genes required for replication is into an E1 deleted region of the vector (shown in Figs. 10 and 11; limitation of claims 12 and 13).

With regard to the limitation of claim 15, wherein the hybrid virus can complete viral replication in a helper cell that provides AAV Rep and Cap, Mountz et al. describe AdAAV viruses that express the cap and rep genes separately , to separately modulate their expression (column, 17, lines 4-7); Additionally teaching the use of a stable cell line which constitutively expresses the rep and cap genes to provide rAAV packaging function (column 19, lines 20-22).

In Example 12, column 18, Mountz et al. state: "The helper-dependent recombinant adenoviruses, including AdrAAV8kb (FIG. 10B) and AdrAAV-GFP8kb (FIG. 10C) which produces high-titer, Ad-free rAAV, was constructed by deleting an 8 Kb PmeI-SgfI fragment encoding the Ad hexon, penton, core protein, and DNA polymerase genes from plasmid pAdAAV or pAdrAAV-GFP (FIG. 1A, FIG. 4A). This virus already has deletions in the E1 and E3 genes. Both constructs are able to replicate and be packaged in the presence of the Ad helper virus, AdLoxpTK, in 293CreNS cells." (limitation of claims 35 and 36).

In Example 4, column 13, Mountz et al. describe the construction of a hybrid AdrAAV vector encoding a GFP protein operably linked to the CMV promoter (the GFP constituting a heterologous reporter polypeptide; limitation of claims 21 and 22, 26 and 27).

The teachings of Lieber et al. and Mountz et al. are both directed to hybrid adeno/AAV vectors. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine their respective teachings and to include a functional adenovirus E4orf6 region in the hybrid vector of Lieber et al., with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would construct such a hybrid adeno/AAV vector as a matter of design choice, which amounts to combining prior art elements according to known methods to yield predictable results. Applicants should note that the *KSR* case forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR International Co. v. Teleflex Inc.*, 550 U.S.-, 82USPQ2d 1385 (2007).

Claims 1 and 21-23 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Lieber et al. (J. Virol. 73(11):9314-9324; 1999), in view of Mountz et al. (U.S. Patent No.: 6,383,794, filed Aug. 24, 1999), as applied to claims 1-3, 5-7, 9, 12-15, 17-22, 26, 27, 35 and 36 above, and further in view of Souza et al. (U.S. Patent Application Publication No.: 2003/0017139; effective filed Nov. 16, 1999).

The claims encompass a recombinant adenovirus/AAV hybrid virus comprising an adenovirus vector genome deleted in the polymerase region, or the preterminal protein region, or both; comprising AAV2 inverted terminal repeats (ITRs) and cis-elements for viral replication, packaging and encapsidation, and a functional adenovirus E4orf6 region, further comprising a heterologous nucleic acid sequence that is operatively associated with a liver-specific promoter, and wherein the AAV genome does not encode the AAV rep or AAV capsid proteins, and wherein the vector genome encodes an AAV rep protein operably linked to the AAV p5 promoter.

Lieber et al. describe integrating adenovirus-AAV hybrid vectors devoid of all viral genes (Title). Further teaching that ITRs inserted into adenovirus (Ad) vector genomes resulting in vector genomes devoid of all viral genes, are efficiently packaged into functional Ad capsids

(Abstract). The Ad vectors contain AAV ITRs flanking a reporter gene cassette; Ad.AAV vector genomes contain only the transgene flanked by AAV ITRs, and packaging signals (Abstract; the reporter transgene corresponding to a heterologous nucleic acid, limitation of claim 1(b)).

In Figure 1, Lieber et al. depict an Ad.AAV2 hybrid vector comprising a neo gene under the control of the SV40 and Tn5 promoters. As the hybrid vector genome does not include coding sequence for any adenoviral or AAV proteins, it necessarily comprises deletions of the adenovirus polymerase and preterminal protein regions (limitation of claim 1(a) (i-iii)). Lieber et al. additionally teach hybrid vectors containing the AAV2 genome ITRs (second column, p. 9315, Figure 1, and first column, first paragraph, p. 9317). The Ad.AAV vectors are described as a promising tool for stable gene transfer *in vitro* and *in vivo* (Abstract).

Mountz et al. disclose high titer recombinant AAV hybrid vectors encoding a therapeutic gene flanked by ITRs of AAV and the AAV rep and cap genes (Abstract). The recombinant AAV further comprises the adenoviral ITRs and an adenovirus packaging signal, El, E2A, E4 and VIA regions and no other adenoviral gene regions (see Fig. 15B, pages 42-44; limitation of claims 2). Mountz et al. state: "Preferably, the adenovirus genome is deleted for all coding sequences other than those genes required for adenoviral replication. More preferably, the genes required for adenoviral replication, and hence remaining on the adenoviral genome, are E1A, E1B, E2A, E4 and VIA." (column 7, last paragraph; limitation of claim 10). As the recombinant hybrid vector does not contain an E2B region, it necessarily is deficient in sequences encoding the preterminal and polymerase protein regions (limitation of claims 1(a) and 17-20). Further, the E4 region contains the E4orf6 (limitation of claim 1(a)). In Example 4, column 13, Mountz et al. describe the construction of a hybrid AdrAAV vector encoding a GFP protein operably linked to the CMV promoter (the GFP constituting a heterologous reporter polypeptide; limitation of claims 21 and 22).

While Lieber et al. and Mountz et al. do not describe their hybrid AAV vectors encoding a heterologous nucleic acid as operatively associated with a liver-specific promoter, such promoters were known in the prior art.

Souza et al. describe adeno-associated viral vectors comprising liver specific

enhancer/promoter combinations linked to a transgene administered to recipient cells (Abstract). The references of Lieber et al., Mountz et al. and Souza et al. are all directed to the use of recombinant AAV vectors for transfer of heterologous transgenes genes to recipient cells. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to use the liver-specific promoter of Souza et al. in the hybrid AAV vector of Lieber et al. or Mountz et al. for gene transfer, with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would be motivated to utilize the hybrid AAV vector of Lieber et al. or Mountz et al. for transfer of transgene operably linked to a liver-specific promoter for therapy, because such vectors could be produced at high titer and high purity (see Abstract, Lieber et al).

Claims 1, 26-28 and 30-33 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lieber et al. (J. Virol. 73(11):9314-9324; 1999), in view of Mountz et al. (U.S. Patent No.: 6,383,794, filed Aug. 24, 1999), as applied to claims 1-3, 5-7, 9, 12-15, 17-22, 26, 27, 35 and 36 above, and further in view of Podsakoff et al. (U.S. Patent No.: 5,962,313; effective filed Jan. 16, 1997).

The claims encompass a recombinant adenovirus/AAV hybrid virus comprising an adenovirus vector genome deleted in the polymerase region, or the preterminal protein region, or both; comprising AAV2 inverted terminal repeats (ITRs) and cis-elements for viral replication, packaging and encapsidation, and a functional adenovirus E4orf6 region, further comprising a heterologous nucleic acid sequence encoding human lysosomal acid α-glucosidase, and wherein the AAV genome does not encode the AAV rep or AAV capsid proteins, and wherein the vector genome encodes an AAV rep protein operably linked to the AAV p5 promoter.

The instant specification identifies glycogen storage disease type II (GSD II) as a classical lysosomal storage disorder, mediated by Acid α-Glucosidase (second paragraph p. 2).

Lieber et al. describe integrating adenovirus-AAV hybrid vectors devoid of all viral genes (Title). Further teaching that ITRs inserted into adenovirus (Ad) vector genomes resulting in vector genomes devoid of all viral genes, are efficiently packaged into functional Ad capsids (Abstract). The Ad vectors contain AAV ITRs flanking a reporter gene cassette; Ad.AAV vector

genomes contain only the transgene flanked by AAV ITRs, and packaging signals (Abstract; the reporter transgene corresponding to a heterologous nucleic acid, limitation of claim 1(b)).

In Figure 1, Lieber et al. depict an Ad.AAV2 hybrid vector comprising a neo gene under the control of the SV40 and Tn5 promoters (constituting a reporter polypeptide; limitation of claims 26 and 27). As the hybrid vector genome does not include coding sequence for any adenoviral or AAV proteins, it necessarily comprises deletions of the adenovirus polymerase and preterminal protein regions (limitation of claim 1(a) (i-iii)). Lieber et al. additionally teach hybrid vectors containing the AAV2 genome ITRs (second column, p. 9315, Figure 1, and first column, first paragraph, p. 9317). The Ad.AAV vectors are described as a promising tool for stable gene transfer *in vitro* and *in vivo* (Abstract).

Mountz et al. disclose high titer recombinant AAV hybrid vectors encoding a therapeutic gene flanked by ITRs of AAV and the AAV rep and cap genes (Abstract). The recombinant AAV further comprises the adenoviral ITRs and an adenovirus packaging signal, El, E2A, E4 and VIA regions and no other adenoviral gene regions (see Fig. 15B, pages 42-44; limitation of claims 2). Mountz et al. state: "Preferably, the adenovirus genome is deleted for all coding sequences other than those genes required for adenoviral replication. More preferably, the genes required for adenoviral replication, and hence remaining on the adenoviral genome, are E1A, E1B, E2A, E4 and VIA." (column 7, last paragraph; limitation of claim 10). As the recombinant hybrid vector does not contain an E2B region, it necessarily is deficient in sequences encoding the preterminal and polymerase protein regions (limitation of claims 1(a) and 17-20). Further, the E4 region contains the E4orf6 (limitation of claim 1(a)).

While Lieber et al. and Mountz et al. do not describe their hybrid AAV vector heterologous protein as human lysosomal acid α-glucosidase, the prior art had taught AAV vectors carrying a nucleic acid encoding for lysosomal acid α-glucosidase.

Podsakoff et al. describe AAV vectors comprising a gene encoding a lysosomal enzyme (Title). In Example 8 (column 27), Podsakoff et al. describe *in vitro* and *in vivo* transduction of muscle cells using a rAAV-hGAA vector encoding human lysosomal acid α-glucosidase to treat

glycogen storage type II (Pompe's disease) (columns 27 and 28; limitation of claims 28 and 30-33).

The references of Lieber et al., Mountz et al. and Podsakoff et al. are all directed to the use of recombinant AAV vectors for transfer of heterologous genes *in vitro* and *in vivo*. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to use the human lysosomal acid α-glucosidase of Podsakoff et al. in hybrid AAV vectors for gene transfer, with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would be motivated to utilize the hybrid AAV vectors for transfer of the human lysosomal acid α-glucosidase transgene for therapy, because such vectors could be produced at high titer and high purity (see Abstract, Lieber et al).

Conclusion

Claims 1-3, 5-7, 9, 12-15, 17-23, 26-28, 30-33, 35 and 36 are not allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. The claims are drawn to the same invention claimed earlier in the application and would have been finally rejected on the grounds and art of record in the next Office Action if they had been entered earlier in the application. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Examiner, Art Unit 1633